10/037,519
LVCook
12/10/04

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(FILE 'HOME' ENTERED AT 14:50:28 ON 10 DEC 2004)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT 14:50:48 ON 10 DEC 2004

L1	1208	S (THIOFLAVIN T)
L2	68	S L1 AND (ALPHA SYNUCLEIN)
L3	52	S L2 AND AGGREGAT?
L4	25	DUPLICATE REMOVE L3 (27 DUPLICATES REMOVED)
L5	0	S L4 AND NM?

Parkinson Disease: PP, physiopathology
Thiazoles: DU, diagnostic use
Tumor Cells, Cultured
Ubiquitins: ME, metabolism

RN 119938-65-7 (synuclein); **2390-54-7 (thioflavin T)**; 7439-89-6 (Iron)

CN 0 (Free Radicals); 0 (Nerve Tissue Proteins); 0 (Thiazoles); 0 (Ubiquitins)

L4 ANSWER 22 OF 25 MEDLINE on STN

AN 1998342238 MEDLINE

DN PubMed ID: 9675319

TI Human recombinant NACP/**alpha-synuclein** is **aggregated** and fibrillated in vitro: relevance for Lewy body disease.

AU Hashimoto M; Hsu L J; Sisk A; Xia Y; Takeda A; Sundsmo M; Masliah E

CS Department of Neurosciences, School of Medicine, University of California-San Diego, La Jolla, CA 92093-0624, USA.

NC AG05131 (NIA)
AG10689 (NIA)

SO Brain research, (1998 Jul 20) 799 (2) 301-6.
Journal code: 0045503. ISSN: 0006-8993.

CY Netherlands

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199809

ED Entered STN: 19981008
Last Updated on STN: 19981008
Entered Medline: 19980925

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CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Hydrogen-Ion Concentration
*Nerve Tissue Proteins: PH, physiology
Nerve Tissue Proteins: UL, ultrastructure
Osmolar Concentration
Parkinson Disease: ET, etiology
Recombinant Proteins
Temperature
Thiazoles: ME, metabolism
Time Factors

RN 119938-65-7 (synuclein); **2390-54-7 (thioflavin T)**

CN 0 (Nerve Tissue Proteins); 0 (Recombinant Proteins); 0 (Thiazoles)

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L1 1208 S (THIOFLAVIN T)
L2 68 S L1 AND (ALPHA SYNUCLEIN)
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L4 25 DUPLICATE REMOVE L3 (27 DUPLICATES REMOVED)
L5 0 S L4 AND NM?

ANSWER 25 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:1021031 CAPLUS
ED Entered STN: 29 Nov 2004
TI Impact of the Acidic C-Terminal Region Comprising Amino Acids 109-140 on .**alpha**.-**Synuclein Aggregation** in Vitro
AU Hoyer, Wolfgang; Cherny, Dmitry; Subramaniam, Vinod; Jovin, Thomas M.
CS Department of Molecular Biology, Max Planck Institute for Biophysical Chemistry, Goettingen, D-37077, Germany
SO Biochemistry ACS ASAP
CODEN: BICHAW; ISSN: 0006-2960
PB American Chemical Society
DT Journal
LA English
CC 6 (General Biochemistry)
AB The **aggregation** of .**alpha**.-**synuclein**, involved in the pathogenesis of several neurodegenerative disorders such as Parkinson's disease, is enhanced in vitro by biogenic polyamines binding to the highly charged C-terminal region aa109-140. In this study, we investigated the influence of this region on the **aggregation** kinetics, monitored by **thioflavin T** binding and static light scattering, and morphol., assessed by electron microscopy, fluorescence microscopy, and turbidity, by comparing the effect of various solution conditions on the wild-type protein, the disease related mutants A53T and A30P, and two truncated variants, syn(1-108) and syn(1-124), lacking the complete or the C-terminal half of the polyamine binding site. In the presence of the intact C-terminus, **aggregation** was strongly retarded in physiol. buffer. This inhibition of **aggregation** was overridden by (i) addition of spermine or MgCl2 or lowering of pH, leading to strong charge shielding in the C-terminus or (ii) by truncation of aa125-140 or aa109-140. Addition of MgCl2 or spermine or acidification were not effective in promoting **aggregation** of syn(1-108). The impact of the disease-related mutations on the **aggregation** kinetics was dependent on the solution conditions, with the **aggregation** propensity order A53T .apprx. wt > A30P at low ionic strength, but A53T > wt .apprx. A30P at high ionic strength, with exceedingly potent promotion of **aggregation** by the A53T mutation in the presence of spermine. In contrast to full-length .**alpha**.-**synuclein aggregates**, those formed from syn(1-108) did not exhibit a pronounced polymorphism. The effects of the C-terminus on **aggregation** cannot be rationalized merely by a contribution to the protein net charge, but rather suggest a specific role of aa109-140 in the regulation of **aggregation**, presumably involving formation of intramol. contacts.

RE.CNT 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Antony, T; J Biol Chem 2003, V278, P3235 CAPLUS
(2) Baba, M; Am J Pathol 1998, V152, P879 CAPLUS
(3) Bussell, R; J Mol Biol 2003, V329, P763 CAPLUS
(4) Chandra, S; J Biol Chem 2003, V278, P15313 CAPLUS
(5) Chiti, F; Nat Struct Biol 2002, V9, P137 CAPLUS
(6) Chiti, F; Nature 2003, V424, P805 CAPLUS
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(9) Conway, K; Biochemistry 2000, V39, P2552 CAPLUS
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(17) Ding, T; Biochemistry 2002, V41, P10209 CAPLUS

ANSWER 25 OF 25 CAPLUS COPYRIGHT 2004 ACS on STN
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ANSWER 22 OF 25 MEDLINE on STN
AN 1998342238 MEDLINE
DN PubMed ID: 9675319
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AU Hashimoto M; Hsu L J; Sisk A; Xia Y; Takeda A; Sundsmo M; Masliah E
CS Department of Neurosciences, School of Medicine, University of California-San Diego, La Jolla, CA 92093-0624, USA.
NC AG05131 (NIA)
AG10689 (NIA)
SO Brain research, (1998 Jul 20) 799 (2) 301-6.
Journal code: 0045503. ISSN: 0006-8993.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
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CT Check Tags: Human; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Hydrogen-Ion Concentration
*Nerve Tissue Proteins: PH, physiology
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Osmolar Concentration
Parkinson Disease: ET, etiology
Recombinant Proteins
Temperature
Thiazoles: ME, metabolism
Time Factors
RN 119938-65-7 (synuclein); **2390-54-7 (thioflavin T)**
CN 0 (Nerve Tissue Proteins); 0 (Recombinant Proteins); 0 (Thiazoles)

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Hydrogen-Ion Concentration
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Time Factors
RN 119938-65-7 (synuclein); **2390-54-7 (thioflavin T)**
CN 0 (Nerve Tissue Proteins); 0 (Recombinant Proteins); 0 (Thiazoles)

ANSWER 21 OF 25 MEDLINE on STN DUPLICATE 10

AN 2000413954 MEDLINE

DN PubMed ID: 10934254

TI The A53T **alpha-synuclein** mutation increases iron-dependent **aggregation** and toxicity.

AU Ostrerova-Golts N; Petrucelli L; Hardy J; Lee J M; Farer M; Wolozin B

CS Departments of Pharmacology, Loyola University Medical Center, Maywood, Illinois 60153, USA.

SO Journal of neuroscience : official journal of the Society for Neuroscience, (2000 Aug 15) 20 (16) 6048-54.
Journal code: 8102140. ISSN: 0270-6474.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 200008

ED Entered STN: 20000907
Last Updated on STN: 20000907
Entered Medline: 20000831

AB Parkinson's disease (PD) is the most common motor disorder affecting the elderly. PD is characterized by the formation of Lewy bodies and death of dopaminergic neurons. The mechanisms underlying PD are unknown, but the discoveries that mutations in **alpha-synuclein** can cause familial PD and that **alpha-synuclein** accumulates in Lewy bodies suggest that **alpha-synuclein** participates in the pathophysiology of PD. Using human BE-M17 neuroblastoma cells overexpressing wild-type, A53T, or A30P **alpha-synuclein**, we now show that iron and free radical generators, such as dopamine or hydrogen peroxide, stimulate the production of intracellular **aggregates** that contain **alpha-synuclein** and ubiquitin. The **aggregates** can be identified by immunocytochemistry, electron microscopy, or the histochemical stain thioflavine S. The amount of **aggregation** occurring in the cells is dependent on the amount of **alpha-synuclein** expressed and the type of **alpha-synuclein** expressed, with the amount of **alpha-synuclein aggregation** following a rank order of A53T > A30P > wild-type > untransfected. In addition to stimulating **aggregate** formation, **alpha-synuclein** also appears to induce toxicity. BE-M17 neuroblastoma cells overexpressing **alpha-synuclein** show up to a fourfold increase in vulnerability to toxicity induced by iron. The vulnerability follows the same rank order as for **aggregation**. These data raise the possibility that **alpha-synuclein** acts in concert with iron and dopamine to induce formation of Lewy body pathology in PD and cell death in PD.

CT Check Tags: Human; Support, Non-U.S. Gov't
Cell Survival: PH, physiology
Free Radicals: ME, metabolism
Inclusion Bodies: ME, metabolism
Inclusion Bodies: UL, ultrastructure
*Iron: TO, toxicity
*Lewy Bodies: ME, metabolism
*Mutation: PH, physiology
Nerve Tissue Proteins: GE, genetics
*Nerve Tissue Proteins: ME, metabolism
Neuroblastoma
Neurons: ME, metabolism
Neurons: PA, pathology
Neurons: UL, ultrastructure
Oxidative Stress: PH, physiology
Parkinson Disease: ET, etiology

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CS Departments of Pharmacology, Loyola University Medical Center, Maywood, Illinois 60153, USA.

SO Journal of neuroscience : official journal of the Society for Neuroscience, (2000 Aug 15) 20 (16) 6048-54.
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CY United States

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Hydrogen-Ion Concentration
*Nerve Tissue Proteins: PH, physiology
Nerve Tissue Proteins: UL, ultrastructure
Osmolar Concentration
Parkinson Disease: ET, etiology
Recombinant Proteins
Temperature
Thiazoles: ME, metabolism
Time Factors
RN 119938-65-7 (synuclein); **2390-54-7 (thioflavin T)**
CN 0 (Nerve Tissue Proteins); 0 (Recombinant Proteins); 0 (Thiazoles)

LVCook
12/10/04
10/037,519

(FILE 'HOME' ENTERED AT 15:38:52 ON 10 DEC 2004)

FILE 'BIOSIS, CAPLUS, EMBASE, MEDLINE, CANCERLIT, JAPIO' ENTERED AT 15:39:10 ON 10 DEC 2004

L1	0	S NACP? AND (THIOFLAVINE T)
L2	384	S (THIOFLAVINE T)
L3	0	S L2 AND NACP?
L4	12	S L2 AND SYNUCLEIN?
L5	4	DUPLICATE REMOVE L4 (8 DUPLICATES REMOVED)
L6	17	S L2 AND (THIOFLAVINE S)
L7	9	DUPLICATE REMOVE L6 (8 DUPLICATES REMOVED)
L8	32	S NAC? AND (THIOFLAVIN T)
L9	16	DUPLICATE REMOVE L8 (16 DUPLICATES REMOVED)
L10	7	S L9 AND AGGREGA?
L11	9	S L9 NOT L10

ANSWER 9 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1967:82948 CAPLUS
DN 66:82948
ED Entered STN: 12 May 1984
TI The histochemistry of azo group-free thiazole dyes
AU Kelenyi, Gabriel
CS Warren State Hosp., Warren, PA, USA
SO Journal of Histochemistry and Cytochemistry (1967), 15(3), 172-80
CODEN: JHCYAS; ISSN: 0022-1554
DT Journal
LA English
CC 6 (Biochemical Methods)
AB Analysis of primuline, **Thioflavine S**, and **Thioflavine T** acid and basic azo group-free thiazole dyes showed that they were built up from a number of components which were characterized by physicochem. methods. The isolated components, as well as related substances of known composition, have characteristic staining properties. Factors involved in the staining mechanism of the dyes and of components, dye concentration, pH, and aggregation of the dye mols., were investigated and their roles are discussed. Selectivity of these fluorescent staining methods was also studied. 19 references.
IT Histochemistry
Staining, biological
(thiazole (azo group-free) dyes in)
IT 92-36-4D, Benzothiazole, 2-(p-aminophenyl)-6-methyl-, derivative 1326-12-1, C.I. Direct Yellow 7 2390-54-7 8064-60-6, C.I. Direct Yellow 59
RL: ANST (Analytical study)
(staining (histochem.) properties of)

=>

ANSWER 3 OF 9 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1998:398875 CAPLUS

DN 129:158068

ED Entered STN: 01 Jul 1998

TI Rapid Assembly of Alzheimer-like Paired Helical Filaments from Microtubule-Associated Protein Tau Monitored by Fluorescence in Solution

AU Friedhoff, Peter; Schneider, Anja; Mandelkow, Eva-Maria; Mandelkow, Eckhard

CS Max-Planck-Unit for Structural Molecular Biology, Hamburg, D-22607, Germany

SO Biochemistry (1998), 37(28), 10223-10230
CODEN: BICHAW; ISSN: 0006-2960

PB American Chemical Society

DT Journal

LA English

CC 6-3 (General Biochemistry)
Section cross-reference(s): 9

AB Alzheimer's disease is characterized by the progressive deposition of two types of fibers in the affected brains, the amyloid fibers (consisting of the Aβ peptide, generating the amyloid plaques) and paired helical filaments (PHFs, made up of tau protein, forming the neurofibrillary tangles). While the principles of amyloid aggregation are known in some detail, the investigation of PHF assembly has been hampered by the low efficiency of tau aggregation, the requirement of high protein concns., and the lack of suitable detection methods. Here we report a quant. assay system that permits monitoring of the assembly of PHFs in real time by the fluorescence of dyes such as **thioflavine S** or T.
Using this assay, we evaluated parameters that influence the efficiency of filament formation. Disulfide-linked dimers of tau constructs representing the repeat domain assemble into PHFs most efficiently, but other tau isoforms or constructs form bona fide PHFs as well. The rate of assembly is greatly enhanced by polyanions such as RNA, heparin, and notably polyglutamate which resembles the acidic tail of tubulin. The assembly is optimal at pH .apprx.6 and low ionic strengths (<50 mM) and increases steeply with temps. above 30 °C, indicating that it is an entropy-driven process.

ST paired helical filaments fluorescence detection tau; PHF assembly tau Alzheimers disease

IT Ionic strength
(effect on rate of polymerization; rapid assembly of Alzheimer-like paired helical filaments from microtubule-associated protein tau)

IT Tau factor
RL: ANT (Analyte); PEP (Physical, engineering or chemical process); ANST (Analytical study); PROC (Process)
(human isoforms htau40 and htau23 and the K19 construct; rapid assembly of Alzheimer-like paired helical filaments from microtubule-associated protein tau)

IT Ionization
(pH dependence on rate of polymerization; rapid assembly of Alzheimer-like paired helical filaments from microtubule-associated protein tau)

IT Organelle
(paired helical filament; rapid assembly of Alzheimer-like paired helical filaments from microtubule-associated protein tau)

IT Aggregation
Fluorescence
(rapid assembly of Alzheimer-like paired helical filaments from microtubule-associated protein tau)

IT Alzheimer's disease
Bioassay
(rapid assembly of Alzheimer-like paired helical filaments from microtubule-associated protein tau monitored by fluorescence in solution)

IT Polarity

Viscosity
(solvent; rapid assembly of Alzheimer-like paired helical filaments from microtubule-associated protein tau)

IT 9005-49-6, Heparin, analysis 25513-46-6
RL: AMX (Analytical matrix); PEP (Physical, engineering or chemical process); ANST (Analytical study); PROC (Process)
(rapid assembly of Alzheimer-like paired helical filaments from microtubule-associated protein tau)

IT 1326-12-1, **Thioflavine S** 2390-54-7, **Thioflavine T**
RL: ARG (Analytical reagent use); PEP (Physical, engineering or chemical process); ANST (Analytical study); PROC (Process); USES (Uses)
(rapid assembly of Alzheimer-like paired helical filaments from microtubule-associated protein tau)

RE.CNT 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD
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ANSWER 5 OF 9 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2000:489305 BIOSIS
DN PREV200000489426
TI Eosin interaction of alpha-synuclein leading to protein self-oligomerization.
AU Shin, Hyun-Ju; Lee, Eun-Kyung; Lee, Ju-Hyun; Lee, Daekyun; Chang, Chung-Soon; Kim, Young-Sik; Paik, Seung R. [Reprint author]
CS Department of Biochemistry, College of Medicine, Inha University, 253 Yonghyun-Dong, Nam-Ku, Inchon, 402-751, South Korea
SO Biochimica et Biophysica Acta, (31 August, 2000) Vol. 1481, No. 1, pp. 139-146. print.
CODEN: BBACAQ. ISSN: 0006-3002.
DT Article
LA English
ED Entered STN: 15 Nov 2000
Last Updated on STN: 10 Jan 2002
AB Among various dyes including congo red, thioflavin S, **thioflavin T**, eosin, rhodamine 6G, and phenol red, the eosin was the only dye that induced self-oligomerization of alpha-synuclein in the presence of a chemical coupling reagent of N-(ethoxycarbonyl)-2-ethoxy-1,2-dihydroquinoline. To analyze chemical nature of the eosin interaction with alpha-synuclein, the phenomenon of self-oligomerization was further examined with eosin congeners such as ethyl eosin, eosin B, phloxine B, erythrosin B, and rose bengal. The followings are the conclusions we have reached. First of all, intactness of the benzoate moiety of eosin and the negative charge on the carboxylic group of the dye are important factors leading to the specific interaction with alpha-synuclein. Secondly, the localized negative charge on the xanthene moiety of eosin is another critical factor for the interaction. As far as substituting halides are concerned, bromides and iodides on the xanthene moiety of the dyes do not make any difference on the alpha-synuclein interaction because both eosin and erythrosin B have induced the common phenomenon of self-oligomerization. The binding curve between eosin and alpha-synuclein was sigmoidal as the dye concentrations were increased. A double reciprocal plot of the saturation curve showed that the maximum number of eosin binding sites on alpha-synuclein was 1.85 with a dissociation constant of 390 muM. The dye binding to the protein appeared to occur via a positive cooperativity. The eosin binding site(s) was suggested to be located predominantly on the **NAC** region and partly related to the acidic C-terminus of alpha-synuclein. It has been, therefore, expected that this information might be useful to develop alpha-synuclein interactive molecules, which could provide eventual preventive or possible therapeutic means against various alpha-synuclein related disorders including Parkinson's disease.
CC Nervous system - Pathology 20506
Biochemistry studies - General 10060
Nervous system - Physiology and biochemistry 20504
IT Major Concepts
Biochemistry and Molecular Biophysics; Nervous System (Neural Coordination)
IT Parts, Structures, & Systems of Organisms
Lewy body: nervous system
IT Diseases
Parkinson's disease: nervous system disease
Parkinson Disease (MeSH)
IT Chemicals & Biochemicals
alpha-synuclein; alpha-synuclein-eosin interaction; eosin
IT Miscellaneous Descriptors
protein self-organization; self-oligomerization
RN 216864-07-2 (alpha-synuclein)
17372-87-1 (eosin)

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Lewy body: nervous system
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alpha-synuclein; alpha-synuclein-eosin interaction; eosin
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